

**RESEARCH REVIEW
ON
MILD TRAUMATIC BRAIN INJURY AND POSTTRAUMATIC STRESS DISORDER**

OVERVIEW

The purpose of this information paper is to provide an overview of the topic of comorbid mild traumatic brain injury (mTBI) and posttraumatic stress disorder (PTSD). This review will focus on symptoms, diagnosis, and treatment of PTSD and mTBI symptoms in patients with mTBI history. While it can be difficult to differentiate symptoms of mTBI from PTSD symptoms, especially months or years after the injury event, this review aims to present information relevant to understanding these often complex cases.

BLUF

While most individuals with mTBI history do not have a comorbid PTSD diagnosis, those who do may present unique challenges. Symptoms of mTBI and PTSD can be similar, and are often more severe in patients with comorbid PTSD and mTBI history than in patients with only one condition. One third or more of deployed OEF/OIF personnel reporting mTBI history also self-report PTSD symptom levels consistent with probable PTSD diagnosis. Some patients in this group experience persistent symptoms and demonstrate reduced neuropsychological test performance, even months or years after injury. Tools for differential diagnosis and determining symptom etiology in the clinical setting are lacking. Neuroimaging approaches offer promise for researchers. There is no evidence that standard PTSD treatments are less effective in patients with mTBI history. Treatments for individuals with PTSD and mTBI history should be directed at specific symptoms regardless of etiology. (Department of Veterans Affairs & Department of Defense, 2017)

DEFINITION AND SYMPTOMS OF MTBI

In the US, an estimated 2.5 million traumatic brain injury (TBI) related emergency department visits occur annually. (Centers for Disease Control and Prevention, 2014) In the last 18 years (January 2000 to December 2017) over 370,000 service members were diagnosed as having had a TBI; 82.3% of those with mTBI. (Defense and Veterans Brain Injury Center, 2018) Approximately 20% of individuals deployed in Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF) report at least one deployment-related TBI. (Tanielian, Jaycox, & Eds., 2008; Terrio et al., 2009)

Mild TBI is defined as a brain injury leading to loss of consciousness of less than 30 minutes, or a confused or disoriented state which persists less than 24 hrs, or post-traumatic amnesia for less than 24 hrs, and normal results on structural computed tomography (CT) scans. (Woodson, 2015) The acute phase of mTBI recovery is defined as the initial seven days after injury, and the chronic phase of recovery is defined as 90 days or more after injury. (Department of Defense & Department of Veterans Affairs, 2009) Symptoms typically resolve without treatment within the first two to four weeks, although a minority of patients experience symptoms for a longer period of time. (Department of Defense & Department of Veterans Affairs, 2009) These symptoms can include: headache, sensitivity to light and sound, malaise, fatigue, irritability, depressed feelings, anxiety, emotional lability, memory and cognitive

impairment, dizziness, and sleep disturbances. (Stein & McAllister, 2009; Vanderploeg, Curtiss, Luis, & Salazar, 2007) Although these symptoms are not unique to mTBI, they are often discussed in the literature as post-concussive symptoms.

DEFINITION AND SYMPTOMS OF PTSD

According to the Institute of Medicine, 13.5% of U.S. Army, 10% of Marines, 4.5% of Navy, and 4% of Air Force service members had PTSD in 2012. Furthermore, over half a million veterans of all conflicts (9.2% of 2012 total VA users) sought VA health services care for PTSD in 2012. (Institute of Medicine of the National Academies, 2014)

PTSD is a psychological condition resulting from exposure to a traumatic event (involving actual or threatened death, serious injury, or sexual violation) characterized by re-experiencing, avoidance, arousal changes, and negative alterations in cognitions and mood, experienced more than one month, and resulting in significant distress or impairment in important area(s) of function. (American Psychiatric Association, 2013) Exposure can include repeated exposure or being personally close to a victim of an event. The symptoms are categorized into four groups: re-experiencing or intrusion; avoidance; arousal; and negative alterations in cognition and mood. PTSD symptoms can include nightmares, flashbacks, distress or arousal at reminders of the trauma, avoidance of conversations about the trauma, avoidance of people or places associated with the trauma, incomplete memory of the trauma, diminished interest in activities, social detachment, emotional numbing, sleep disturbances, irritability, difficulty concentrating, hypervigilance, reckless behavior, or exaggerated startle response. (American Psychiatric Association, 2013; Department of Veterans Affairs & Department of Defense, 2017) Symptoms occurring earlier than one month post-trauma are referred to as acute stress disorder. (American Psychiatric Association, 2017) The DSM-V recognizes PTSD with delayed expression, in which full diagnosis criteria are not met until six months or more post-trauma. (Sayer, Nelson, & Nugent, 2011)

PREVALENCE OF COMORBID MTBI AND PTSD

Experiencing a traumatic event that causes TBI may also initiate a constellation of symptoms which secondarily lead to post-traumatic stress disorder (PTSD). However, PTSD can predate injury, arise concurrently or after onset of post-concussive symptoms, or relate to a separate event or series of events. Most literature on comorbid PTSD with military-related mTBI history does not address preexisting trauma or premorbid PTSD symptoms. One prospective, longitudinal study showed that pre-deployment PTSD symptoms were positively correlated with similar symptoms post-deployment regardless of TBI status. (Yurgil et al., 2014)

Depending on the population under study, the prevalence of co-morbid PTSD and TBI can vary greatly. (Carlson et al., 2011) Among military and veteran populations, most studies report the prevalence of PTSD as 10-40% of study participants with probable or diagnosed history of TBI. (Carlson et al., 2011; Hill, Mobo, & Cullen, 2009; Hoge et al., 2008; Kontos et al., 2013; Schneiderman, Braver, & Kang, 2008; Tanielian et al., 2008) Prevalence can be higher in treatment-seeking samples as compared to non-treatment-seeking samples. (Ramchand, Rudavsky, Grant, Tanielian, & Jaycox, 2015)

Risk factors for PTSD after mTBI

The risk of PTSD is elevated two to three fold after mTBI, according to studies of veterans, service members, and civilians. (Bryant et al., 2010; Miller et al., 2015; Schneiderman et al., 2008; Stein et al., 2015; Vanderploeg et al., 2012; Yurgil et al., 2014) Those who experience mTBI with loss of consciousness (LOC) may be at higher risk of developing PTSD (Eskridge et al., 2013; Hoge et al., 2008; Norris, Sams, Lundblad, Frantz, & Harris, 2014) or having more severe PTSD symptoms (Sofko, Currier, Hill, & Drescher, 2016) as compared to those with mTBI without LOC.

Risk factors for PTSD after trauma have been determined empirically, and fall into three categories: preexisting, trauma-related, and posttraumatic. Preexisting risk factors include low IQ, prior trauma exposure (especially childhood abuse or adversity (Brewin, Andrews, & Valentine, 2000)), and prior psychological disorder. Trauma-related risk factors include perceived fear of death and physical injury. Posttraumatic factors that increase risk of PTSD include low social support, pain severity, and peritraumatic dissociation (reduced awareness or altered perceptions during and immediately after the trauma). (Ozer, Best, Lipsey, & Weiss, 2003; Sareen, 2014)

A recent systematic review of studies on mental health after deployment to Iraq or Afghanistan found several characteristics were associated with increased risk of PTSD, regardless of TBI status. Those include demographic characteristics, military characteristics, deployment-related factors, pre-deployment factors, and post-deployment factors. (Ramchand et al., 2015) Demographic characteristics associated with an increased risk of PTSD were: age under 40 (for males only), lower education, and unmarried status. Military characteristics associated with an increased risk of PTSD were: serving in the US Army or Marines (as compared to serving in other US services); enlisted rank; and health-care occupations, combat specialists, and service and supply personnel (as compared to other occupational specialties). Deployment-related characteristics associated with an increased risk of PTSD were a higher number of deployments and any injury sustained in combat. Pre-deployment factors associated with a higher risk of PTSD diagnosis were: life stress, childhood adversity or vulnerability, poorer perceptions of preparedness, and pre-deployment PTSD symptoms. PTSD was also associated with poor post-deployment social support and post-deployment life stressors. Ramchand et al. did not find a gender difference in PTSD risk after deployment to Iraq or Afghanistan, but in civilian studies, women are at increased risk of PTSD. (Brewin et al., 2000)

Population characteristics

PTSD with mTBI history in service members and veterans is often associated with other psychological or physical conditions. (Blakey et al., 2018; Jaramillo et al., 2016; Lew et al., 2009; Sayer et al., 2009) Specifically, depression, headache, suicidal impulses, substance use disorder, pain, cumulative disease burden, and polypharmacy have been documented in this population. (Blakey et al., 2018; Gros, Lancaster, Horner, Szafranski, & Back, 2017; Hoge et al., 2008; Isaac et al., 2015; Jaramillo et al., 2016; Morgan, Lockwood, Steinke, Schleenbaker, & Botts, 2012; Stojanovic et al., 2016; Williams, McDevitt-Murphy, Murphy, & Crouse) Social outcomes reported in the PTSD and mTBI population include reduced psychosocial function, driving problems, missed work, and experiencing intimate partner violence. (Hoge et al., 2008; Iverson, Dardis, & Pogoda, 2017; Jackson et al., 2016; Van Voorhees et al., 2018) Evidence

shows that veterans with persistent symptoms after mTBI can have greater healthcare and medication use. (King, Wade, & Beehler, 2014; Morgan et al., 2012)

UNCLEAR SYMPTOM ETIOLOGY

Evidence suggests that PTSD and mTBI symptoms are correlated and difficult to distinguish. A number of studies have shown that PTSD symptoms are more severe in military and veteran groups with probable or diagnosed mTBI than those with no TBI. (Combs et al., 2015; Mac Donald et al., 2015; Spira, Lathan, Bleiberg, & Tsao, 2014; Vanderploeg, Belanger, & Curtiss, 2009) PTSD is associated with post-concussive symptoms in military and veteran populations. (Brenner et al., 2010a; Cernich, Chandler, Scherdell, & Kurtz, 2012; Dretsch, Silverberg, & Iverson, 2015; Schneiderman et al., 2008; Waldron-Perrine, Hennrick, Spencer, Pangilinan, & Bieliauskas, 2014) In some studies with military or veteran participants more than 3 months after TBI, psychological factors were more predictive of post-concussive symptoms than TBI status. (Hoge et al., 2008; Polusny et al., 2011; Ponsford et al., 2012; Porter et al., 2018; Verfaellie, Lafleche, Spiro, Tun, & Bousquet, 2013) In the acute phase of injury, one study of service members showed that acute stress reaction may partially mediate post-concussive symptoms. (Norris et al., 2014)

Post-concussive symptoms also occur at a high base rate in uninjured civilians, (Wang, Chan, & Deng, 2006) and can arise from multiple etiologies. (Vanderploeg et al., 2012; Waldron-Perrine et al., 2014) As noted above, post-concussive symptoms have been associated with psychological conditions independent of TBI among active duty, veteran, deployed Guard, and civilian populations. (Dretsch et al., 2015; Hoge et al., 2008; Iverson & Lange, 2003; Porter et al.; Soble et al., 2014; Waldron-Perrine et al., 2014) Post-concussive symptoms are also associated with non-TBI injuries among veterans. (Vanderploeg et al., 2012) Studies that have attempted to differentiate symptom patterns between PTSD and mTBI have not had consistent results. (Maugen, Lau, Madden, & Seal, 2012; Polusny et al., 2011)

NEUROPSYCHOLOGICAL FUNCTION

Objective evaluations of post-concussive symptoms are important for determining return-to-duty, benefits, and other decisions. Tests of executive and motor function, memory, attention, learning, and other domains can provide objective assessments. Neuropsychological impairment can be present in the absence of self-reported cognitive symptoms, or absent in the presence of self-reported cognitive symptoms. (French, Lange, & Brickell, 2014a)

Comorbid group

Multiple studies in OEF/OIF veteran and service member populations with PTSD and mTBI history have shown that neuropsychological outcomes can be negatively impacted months or years after injury. Several studies have shown that those with a PTSD diagnosis or significant PTSD symptoms in combination with reported mTBI history performed significantly worse on neuropsychological tests as compared to those with PTSD-only, mTBI only, or controls. This has been seen in different populations, including: service members, (Betthausen et al.; Vasterling et al., 2012) veterans (Amick et al., 2013; Barlow-Ogden & Poynter, 2012; Combs et al., 2015; Nelson, Yoash-Gantz, Pickett, & Campbell, 2009; Nelson et al., 2012) and civilians. (Pineau, Marchand, & Guay, 2014)

In contrast, some studies have found no significant neuropsychological differences between those with mTBI history and PTSD and those with only one condition. (Brenner et al., 2010b; Gordon, Fitzpatrick, & Hilsabeck, 2011; Karr, Areshenkoff, Duggan, & Garcia-Barrera, 2014; Soble et al., 2014) A norms-based comparison of veterans with PTSD/mTBI or mTBI history only showed that both groups demonstrated normal cognitive performance. (Soble, Spanierman, & Fitzgerald Smith, 2013) A meta-analysis performed by Karr, et al. did not show a significant difference between PTSD status groups, but was limited in power. (Karr et al., 2014) The inconsistency in findings between these and the above-cited works may be due to participant population, study design, outcomes, or other factors.

Mild TBI Only

During the acute phase of mTBI recovery, decreases in neuropsychological test performance have been observed in civilian settings (McCauley et al., 2014; Peterson, Stull, Collins, & Wang, 2009), and are considered common. (Petrie et al., 2014) A systematic review of civilian studies showed that most mTBI patients recover from neuropsychological impairments within 1-3 months. (Carroll et al., 2004) Studies of acute mTBI patients in the deployed setting are limited and typically do not involve neuropsychological outcomes.

Mild TBI patients in the chronic phase of recovery without comorbid psychological health conditions do not consistently demonstrate poorer neuropsychological test performance as compared to non-TBI controls. Several studies of OEF/OIF veterans assessed several years after mTBI have found no neuropsychological differences between those with mTBI only and controls without mTBI. (Amick et al., 2013; Dretsch et al., 2015; Nelson et al., 2012; Shandera-Ochsner et al., 2013; Verfaellie, Lafleche, Spiro, & Bousquet, 2014)

The finding that mTBI alone has no lasting neuropsychological outcomes is not universal. A recent meta-analysis by Karr et al. of nine studies of cognitive function at least 90 days after military-related mTBI in veterans and deployed persons found subtle, chronic cognitive impairments associated with mTBI. (Karr et al., 2014) The meta-analysis may have been able to detect smaller changes than the individual studies. However, a number of these studies had small participant numbers, and several included participants who had sustained a high number of mTBIs. Patients with a history of multiple mTBIs may be at higher risk of chronic cognitive and functional impairment. (Morey et al., 2013)

PTSD Only

PTSD alone is associated with decreased neurocognitive test performance in several domains, especially verbal learning, speed of information processing, and attention/ working memory, according to a recent meta-analysis including data from 1,779 PTSD patients. This meta-analysis included a mixture of studies of military and other trauma survivors. (Scott et al., 2015) These findings are consistent with neuropsychological studies showing reduced performance in veterans with PTSD as compared to veteran controls. (Nelson et al., 2012; Shandera-Ochsner et al., 2013; Swick, Honzel, Larsen, Ashley, & Justus, 2012)

In addition to the group-based findings described above, researchers have also found correlations between neuropsychological outcomes and PTSD symptoms (Vasterling et al., 2012; Verfaellie et al., 2014) or diagnosis. (Larson, Zollman, Kondiles, & Starr, 2013) Taken together,

these data suggest that PTSD and subclinical PTSD symptoms may be driving cognitive impairments observed among PTSD patients with mTBI history.

OTHER DIAGNOSTIC AND ASSESSMENT TOOLS

Assessment of PTSD and mTBI based on symptoms alone can be difficult due to the significant overlap, and lack of tools for understanding symptom etiology. This section describes common diagnostic and assessment tools relevant to both conditions.

The Neurobehavioral Symptom Inventory (NSI) and the Rivermead Post-concussion Symptoms Questionnaire (RPQ) are patient reporting tools that can be used to determine symptom severity. (Cicerone & Kalmar, 1995; Kaplan, 2014; King, Crawford, Wenden, Moss, & Wade, 1995) The two instruments are similar in that they provide a list of symptoms (22 on the NSI, 16 on the RPQ) and ask test takers to indicate severity on a five-point scale. The NSI also has two items that invite the test-taker to name a symptom and provide a severity rating. Several factor analysis studies have been performed that seek to group symptoms to improve interpretation of results. (Benge, Pastorek, & Thornton, 2009; Caplan et al., 2010; Franke, Czarnota, Ketchum, & Walker, 2015; Vanderploeg et al., 2015) The resulting factor structures vary, but one comparative analysis found that a factor structure including four (vestibular, somatic, cognitive, and affective) provided the best fit for a sample of deployed Guard and veterans. (Vanderploeg et al., 2015)

Neither the NSI nor the RPQ are diagnostic, in part due to the high base rate of these symptoms among uninjured populations (Iverson & Lange, 2003; Wang et al., 2006), and in part because a number of symptoms on these scales also associate with PTSD and other psychological conditions. For PTSD diagnosis, the gold standard is the clinician-administered PTSD scale (CAPS) (Weathers, Keane, & Davidson, 2001), and tools including the PTSD Checklist (PCL-M and PCL-C) that assess symptom severity. (Forbes, Creamer, & Biddle, 2001) Mild TBI diagnosis is based on injury event criteria, including no more than 30 min of LOC. (Department of Defense & Department of Veterans Affairs, 2009)

The VA/DoD Clinical Practice Guideline for PTSD indicates that “all new patients should be screened for symptoms of PTSD initially and then on an annual basis or more frequently if clinically indicated due to clinical suspicion, recent trauma exposure (e.g., major disaster), or history of PTSD.” (Department of Veterans Affairs & Department of Defense, 2017) The DoD includes screening for PTSD in the PDHA and post-deployment health reassessment (PDHRA). (Institute of Medicine of the National Academies, 2014) The most commonly used instrument in the VA and DoD is the Primary Care PTSD Screen (PC-PTSD). (Institute of Medicine of the National Academies, Committee on the Assessment of the Readjustment Needs of Military Personnel Veterans and Their Families, & Board on the Health of Select Populations, 2013) The PC-PTSD is a screen designed for use in primary care and other medical settings. (Prins, 2003) The four questions on the screen relate to avoidance, arousal, vigilance, dissociation, and nightmares. If the patient responds “yes” to any question, that is regarded as a positive screen. (National Center for PTSD, 2015)

Since post-concussive symptom and PTSD symptom instruments are mostly self-report, most tools for assessing mTBI and PTSD are limited because of psychological factors and contextual factors; secondary gain such as disability benefits can also influence responses.

(Betthauser, Bahraini, Kregel, & Brenner, 2012) A study of veterans recruited from forensic, clinical, and research settings found that those with active disability claims were four times more likely to exaggerate symptoms. (Nelson et al., 2011) A systematic review by Carroll et al. of literature regarding civilian mTBI also noted that litigation and compensation are predictive of poor outcomes in cases with disability or persistent symptoms after mTBI. (Carroll et al., 2004)

Approaches other than self-report scales and interviews can detect differences between mTBI, PTSD, and comorbid groups, but are not currently used to diagnose individual patients. For example, neurocognitive tests are meant to test cognitive performance rather than diagnose mTBI. In addition, they are subject to poor effort and memory malingering. (Nelson et al., 2011; Verfaellie et al., 2014) There is current interest in assessments of vestibular and motor function in persons with PTSD and/or mTBI history. (Haber, Chandler, & Serrador, 2016; Kontos et al., 2017) Technologies including fluid biomarkers, (Ho et al., 2014) electroencephalography, (Franke, Walker, Hoke, & Wares, 2016) and magnetoencephalography (Rowland et al., 2018) have been used to characterize subjects with PTSD and/or mTBI, but these approaches are not currently used in the clinical setting.

Imaging Approaches

Traditional computed tomography (CT) scans and magnetic resonance imaging (MRI) cannot differentiate mTBI history alone from mTBI comorbid with PTSD. Researchers have used sophisticated imaging approaches including functional magnetic resonance imaging (fMRI) (McDonald, Saykin, & McAllister, 2012; Roy et al., 2010) and diffusion tensor imaging (DTI) (Bazarian et al., 2013) to investigate the pathology of mTBI and comorbid PTSD with mTBI history. These approaches are not generally available in the clinical setting, and current evidence does not support use for diagnostic or prognostic purposes.

DTI demonstrates diagnostic and prognostic potential, but is not currently used in routine clinical practice. (Hulkower, Poliak, Rosenbaum, Zimmerman, & Lipton, 2013) A number of studies have found differences in DTI parameters between service members with and without PTSD in an mTBI context. (Bazarian et al., 2013; Davenport, Lim, & Sponheim, 2015a, 2015b; Yeh et al., 2014) Other DTI studies have failed to find differences between groups with and without PTSD. (Costanzo et al., 2014; Levin et al., 2010; Matthews, Spadoni, Lohr, Strigo, & Simmons, 2012; Morey et al., 2013; Petrie et al., 2014) PTSD has been found to interact with mTBI in ways that alters DTI parameters in a study of civilians and deployed service members. (Davenport et al., 2016) Further investigations will provide etiological insights and clarify the diagnostic and prognostic value of this technology.

Other imaging approaches that may warrant further study include advanced MRI approaches and single photon emission computed tomography (SPECT). Several studies and a meta-analysis have found fMRI features that were significantly different between those with PTSD and those without. (Roy et al., 2010; Simmons & Matthews, 2012; Spielberg, McGlinchey, Milberg, & Salat, 2015) Limited evidence shows the potential of SPECT to provide diagnostic information in those with PTSD, mTBI history, or both. (Amen et al., 2015; Raji et al., 2015) Brain volume measurements have demonstrated promise for identifying those with comorbid PTSD and mTBI history. (Depue et al., 2014; Lindemer, Salat, Leritz, McGlinchey, & Milberg, 2013) Fluid-attenuated inversion recovery (FLAIR) MRI approaches have also been used to characterize white matter hyperintensity in these populations. (Clark et al., 2016)

While imaging approaches are revealing valuable mechanistic and neuroanatomical information, relevant predictive and diagnostic capabilities remain to be demonstrated in larger clinical samples. Imaging studies are not the current clinical standard in diagnosing PTSD or mTBI.

TREATMENT IMPLICATIONS

Clinical practice guidelines

The VA/DoD treatment guidelines for mTBI three months or more post-injury focus on symptom management, education, and evidence-based diagnosis and treatment of possible comorbid conditions. (Department of Veterans Affairs, Department of Defense, & The Management of Concussion/mTBI Working Group, 2016) Effective treatments for PTSD are in wide dissemination across the VA and DoD. The VA/DoD Clinical Practice Guidelines for PTSD emphasize a collaborative treatment approach, manualized trauma-focused psychotherapy, and recognition of possible comorbid conditions. (Department of Veterans Affairs & Department of Defense, 2017) Interviews conducted by Sayer et al. with VA clinicians revealed a treatment challenge in that providers treating PTSD can prescribe medications contraindicated in patients with mTBI history, or vice versa. (Sayer et al., 2009) These data emphasize the importance of integrated care. Patient retention can also be a treatment challenge. (Fleming, Kholodkov, Dillon, Belvet, & Crawford, 2018; Steenkamp, Litz, Hoge, & Marmar, 2015)

Evidence regarding non-pharmacological interventions

A recent systematic review by Steenkamp et al. on psychotherapy for military-related PTSD found the treatments with the highest evidence recommendations in clinical guidelines were cognitive processing therapy (CPT), trauma-focused exposure therapies, and eye movement desensitization and reprocessing (EMDR) therapy. (Steenkamp et al., 2015) Studies in populations with comorbid PTSD and TBI history show that prolonged exposure therapy is successful in reducing symptoms regardless of their presumed origin. (Sripada et al., 2013; Wolf, Strom, Kehle, & Eftekhari, 2012)

While PTSD treatments are well-supported by evidence, fewer studies have been performed with comorbid PTSD/ mTBI patients. Studies of exposure therapy, (Gros et al., 2017; Roy et al.; Wolf et al., 2015; Wolf et al., 2018), cognitive processing therapy (CPT), (Walter, Dickstein, Barnes, & Chard) and a mindfulness intervention (Cole et al.) have had positive results. Cognitive rehabilitation interventions have reduced psychiatric symptoms in several studies. (Cooper et al., 2017; Cooper et al., 2015; Cooper et al., 2018; Janak et al., 2015; Walter, Jak, & Twamley, 2015) Hyperbaric oxygen treatment has not shown promising results, (Cifu, Hart, West, Walker, & Carne, 2014; Wang, Wang, Sun, & Yu, 2016; Weaver et al., 2018; Wolf, Cifu, Baugh, Carne, & Profenna, 2012), and is discussed in more detail in another information paper. (Qashu, 2015)

Evidence regarding pharmacological interventions

Few studies have been performed with pharmacological therapies specifically for patients with comorbid PTSD and mTBI. (Sayer et al., 2009) A 2009 study by Ruff et al. prospectively studied 74 veterans identified at a VA Polytrauma Center who had sustained blast-related mTBI 2.2 years earlier, on average (96% also had a PTSD diagnosis). (Ruff, Ruff, & Wang, 2009) This

uncontrolled pilot study found that prazosin, in combination with sleep hygiene counseling, reduced daytime sleepiness, headache frequency, and headache pain intensity, and improved scores on a cognitive assessment after 9 weeks. After 6 months, those who stayed on prazosin (n = 64) had maintained gains in symptom reduction and showed further improvement on the cognitive assessment. Clinical improvements were correlated with reduced PTSD symptoms. (Ruff, Riechers, Wang, Piero, & Ruff, 2012) A recent study by McAllister et al. suggested methylphenidate (a central nervous system stimulant) can reduce PTSD, depression, cognitive, and post-concussion symptoms in a mixed military and civilian population with mTBI, PTSD, or comorbid mTBI/PTSD. (McAllister et al., 2016)

Factors protective against PTSD symptoms

Some factors have been identified as providing protective effects for psychological health. A study by Bryant et al. including 459 civilian mTBI patients showed that those with longer duration of post-traumatic amnesia had less severe re-experiencing symptoms when assessed during the acute phase of injury, but overall PTSD symptoms did not differ. (Bryant et al., 2009a) These data indicate that post-traumatic amnesia may be protective against some PTSD symptoms. A study of 46 civilians monitored during the acute phase of mTBI showed that resilience and positive mood as assessed on the day of injury were associated with less severe stress and post-concussive symptoms during the month following injury. (McCauley et al., 2013) Among service members in Afghanistan evaluated for acute concussion, return to duty was associated with the absence of combat stress reaction at the time of injury. (Kennedy et al., 2012) Additionally, two studies have found that comorbid physical injuries, and, perhaps, the associated recovery and rehabilitation, can have a protective effect against post-concussive symptoms and psychological health sequelae in patients with mTBI history. (French et al., 2012; French et al., 2014b) However, patients in these studies were evaluated within about three months of injury, and PTSD can develop later (Grieger et al., 2006) and symptoms may have been dampened at assessment by morphine administration. (Bryant, Creamer, O'Donnell, Silove, & McFarlane, 2009b)

DISCUSSION

Comorbid PTSD and mTBI history cases are often challenging and complex, with some patients presenting more severe or persistent symptoms than individuals without mTBI or with mTBI alone. Published findings regarding long-term neuropsychological function in comorbid PTSD and mTBI patients are not consistent.

Since mTBI and PTSD symptoms are often similar, differential diagnosis will likely continue to be a challenge, although neuroimaging techniques and other biomarkers may provide new diagnostic tools. Evidence shows that standard PTSD treatments can be effective in this population despite challenges cited by clinicians. Further research on mTBI may reveal more effective treatment options and diagnostic tools that benefit patients with PTSD and mTBI history.

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